

REMARKS

The amendment to the specification is made in accordance with 35 U.S.C. 119, 37 C.F.R. 1.78 and 37 C.F.R. 1.55. Claims 113-122 are pending in the application. No new matter has been added. Entry is requested.

This Preliminary Amendment, including claims 113-122, is submitted in order to present for examination subject matter described in the subject application directed to methods for attaching monomers at specific reaction sites on a substrate.

The methods are supported, *inter alia*, throughout the disclosure and/or cited references incorporated by reference.

The specification discloses a method of attaching monomers at specific reaction sites on a substrate (light-directed synthesis of oligonucleotides that employs 5'-protected nucleosidephosphoramidite "building blocks" (page 1, lines 23-24), coupling (i.e., nucleotide or monomer additions) occurs at sites that have been deprotected (page 1, lines 27-28).

The specification discloses specific reaction sites containing one or more non-photolabile protected initiating moieties: polymer array synthesis processing performed using photoacid generators as taught in U.S. Application No. 08/969,227 (U.S. Patent 6,083,697, incorporated by reference) (page 12, lines 17-19), USSN 08/969,227 discloses linker molecules having reactive functional groups protected by protecting groups provided on the surface of a substrate (col. 10, lines 41-44, US Pat No. 6,083,697, incorporated by reference).

The specification discloses contacting the substrate with a liquid solution comprising one or more photo-reagent precursors, the precursors selected from the group consisting of acid and base precursors, such that the liquid solution is in contact with the initiating moieties (claim 113): synthesizing nucleic acid arrays with a photochemical process (page 12, line 21) using photoacid generators (page 13, lines 1-2). For example, p-nitrobenzyltosylate may be used to photochemically generate toluenesulfonic acid (page 13, lines 4-5); p-nitrobenzyltosylate and 2-ethyl-9,10-dimethoxy-anthracene may be used to generate an acid (toluenesulfonic acid) wherein the sensitizer absorbs the light and then transfers the energy to the p-nitrobenzyltosylate, causing dissociation and subsequent release of toluensulfonic acid (page 13, lines 4-10); polymer array synthesis processing performed using photoacid generators as taught in U.S. Application No. 08/969,227 (U.S. Patent 6,083,697) (page 12, lines 17-19), USSN 08/969,227 discloses solutions containing a photo-activated catalyst and an enhancer are spin coated on the surface of the substrate (col. 10, lines 44-45 and col. 18, lines 64 – col. 19, line 5 and col. 19, lines 53-59, US Pat No. 6,083,697, incorporated by reference).

The specification discloses isolating the specific reaction sites (claim 113): light for synthesis of a polymer array reaches certain regions of a substrate but not others (page 2, lines 7-8).

The specification discloses irradiating a selected number of the isolated reaction sites to produce, in situ, at least one photo-generated reagent without the formation of a polymeric coating layer, thereby directly deprotecting the initiating moieties at the irradiated reaction sites so as to create deprotected initiating moieties: micromachined

mechanical modulators direct light to predetermined regions of the substrate on which the polymers are being synthesized (page 6, lines 18-21); in each predetermined region a particular oligonucleotide sequence is synthesized (page 7, lines 1-2); polymer array synthesis processing can be performed using direct photodeprotection without using any photoresist (page 12, lines 15-18); a set of selected regions on the surface of the substrate is exposed to radiation using lithographic methods (col. 10, lines 45-47 in US Pat. No. 6,136,269, incorporated by reference); the PAC catalyst activated by the region-selective irradiation acts to initiate a reaction of the enhancer which produces at least one product that removes the protecting groups from the linker molecules in the first selected regions (col. 10, lines 52-56 in US Pat. No. 6,136,269, incorporated by reference).

The specification discloses contacting the substrate with a first monomer, the first monomer comprising an unprotected reactive site and a protected reactive site, under conditions such that the unprotected reactive site of the monomer couples with the deprotected initiating moieties so as to create an attached first monomer: polymer array synthesis processing performed using photoacid generators as taught in U.S. Application No. 08/969,227 (U.S. Patent 6,083,697) (page 12, lines 17-19), USSN 08/969,227 discloses monomers for synthesis of polymers where each set of monomers includes protected members which are modified after synthesis (col. 5, lines 40-45, US Pat No. 6,083,697, incorporated by reference).

The specification discloses initiating moieties (claim 114) that comprise linker molecules, each of the linker molecules comprising a reactive functional group protected by an acid-labile protecting group: polymer array synthesis processing performed using

photoacid generators as taught in U.S. Application No. 08/969,227 (U.S. Patent 6,083,697) (page 12, lines 17-19), USSN 08/969,227 discloses linker molecules having reactive functional groups protected by protecting groups provided on the surface of a substrate (col. 10, lines 41-44, US Pat No. 6,083,697, incorporated by reference).

The specification discloses the method where the reactive functional group of the linker molecules comprises a hydroxyl group (claim 115) and the monomer is selected from the group consisting of nucleophosphoramidites, nucleophosphonates and analogs thereof (claim 116): the monomer is a 2'deosynucleoside phosphoramidite containing an acid removable protecting group at its 5' hydroxyl group. (col. 11, lines 7-10, U.S. Pat No. 6,083,697, incorporated by reference).

The specification discloses the monomer comprises a nucleotide monomer with a protected group (claim 117) and the protected group is protected by an acid-labile group (claim 118): the monomer may be a 2'deoynucleoside phosphoramidite containing an acid removable protecting group at its 5' hydroxyl group (col.11,lines 8-10, US Pat No. 6,083,697, incorporated by reference).

The specification discloses the step of deprotecting the protected group so as to create a deprotected attached nucleotide monomer (claim 119): the substrate is then contacted with a first monomer that reacts with exposed functional groups on linker molecules (col. 10, lines 58-60, US Pat No 6,083,697, incorporated by reference); radiation-initiated reactions remove protecting groups on molecules in a second set of selected regions, i.e., the linker molecules and the *first-bound monomers* (col. 10, lines 63-66, US Pat No. 6,083,697, incorporated by reference); the substrate is then contacted

with a second monomer containing a removable protective group for reaction with exposed functional groups (col. 10, lines 66 – col. 11, lines 1, US Pat No. 6,083,697, incorporated by reference).

The specification discloses the step of contacting the deprotected attached nucleotide monomer with a second monomer (claim 120): polymer sequences in predefined regions are synthesized by repeated cycles of deprotection and coupling (page 1, lines 25-27); coupling (i.e., nucleotide or monomer additions) occurs at sites that have been deprotected (page 1, lines 27-28); the substrate the substrate is then contacted with a second monomer containing a removable protective group for reaction with exposed functional groups (col. 10, lines 66 – col. 11, lines 1, incorporated by reference).

The specification discloses the second monomer comprising an unprotected reactive site and a protected reactive group and conditions such that the unprotected reactive site of the second monomer couples with the deprotected attached nucleotide monomer so as to create an attached second monomer, the attached first and second monomers comprises a multimer (claim 120): polymer sequences in predefined regions are synthesized by repeated cycles of deprotection and coupling (page 1, lines 25-27); coupling (i.e., nucleotide or monomer additions) occurs at sites that have been deprotected (page 1, lines 27-28); the linker, having a newly exposed reactive group, is contacted with a monomer capable of reacting with the linker. The monomer also has a protective group which can be removed in a subsequent reaction step. In this step wise manner, diverse arrays of polymers are synthesized at preselected regions of a substrate (col. 10, lines 1-7, US Pat No. 6,083,697, incorporated by reference); a second monomer

contains a removable protective group for reaction with exposed functional groups (col. 10, line 66 – col. 11, line 1, US Pat No. 6,083,697, incorporated by reference).

The specification discloses the multimer comprises DNA (claim 121): nucleic acid sequences can also be immobilized in specific location or predefined regions of a substrate (col. 9, lines 41-42, US Pat No. 6,083,697, incorporated by reference).

The specification discloses the initiating moieties comprise oligomers to which a monomer can be attached (claim 122): useful linker molecules include ... oligomers of nucleotides ... and the like (col. 11, lines 36-40, US Pat No. 6,083,697, incorporated by reference).

Notification of copied claims from U.S. Patent No. 6,426,184 pursuant to 37 C.F.R. 1.607(c)

This Amendment is accompanied by an Information Disclosure Statement and prompt consideration of that Statement also is requested. U.S. Patent No 6,426,184, listed in the Statement, claims a method of attaching monomers at specific reaction sites on a substrate. Claims 113-122 of the present application have been copied from U.S. Patent 6,426,184. Specifically, Claims 113-122 of the present application correspond in scope and content to U.S. Patent 6,426,184, claims 1-9 and 11, respectively. The effective filing date of the application is more than three months after the effective filing date of U.S. Patent No. 6,426,184.

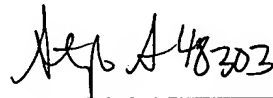
Applicants are filing the present amendment presenting claims copied from U.S. Patent 6,426,184 within one year of the issue date of U.S. Patent 6,426,184 to preserve

the right to request an interference pursuant to 35 U.S.C. 135. However, Applicants do *not* presently request an interference, pending an indication of allowability by the Examiner on Applicant's right to make the copied claims. Before an interference may be declared between an application and an unexpired patent, an examiner must determine that there is interfering subject matter claimed in the application and the patent which is patentable to the applicant subject to a judgment in the interference. The application must contain, or be amended to contain, at least one claim that is patentable over the prior art supported by the application and corresponds to each count. 37 C.F.R. § 1.606.

Therefore, prior to requesting an interference and pending the indication of otherwise allowable subject matter and the determination by the Examiner of interfering subject matter, Applicants will submit at a future date, pursuant to 37 C.F.R. § 1.608, evidence demonstrating *prima facie* entitlement to priority of invention with respect to U.S. Patent 6,426,184.

On the basis of the foregoing, consideration of all claims in the subject application is respectfully requested.

Respectfully submitted,



 Pamela Banner Krupka
Registration No. 33,644

BANNER & WITCOFF, LTD.
1001 G Street, N.W.
Washington, D.C. 20001
(202) 508-9100

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